July 3, 2023

*World Journal of Gastrointestinal Oncology*

Dear Editor,

Thanks for your kind letter and advice. We also thank the reviewers for their valuable comments and suggestions. We have revised the manuscript entitled "***Update and Latest Advances in Mechanisms and Management of Colitis-associated Colorectal Cancer***" (Manuscript NO.: 84869, Review) according to the reviewers' and editor's suggestions and carefully proofread the manuscript. Below is our description of the revisions made in response to the reviewers' and editor's comments, and the amendments are showen in red in the revised manuscript. In addition, this manuscript has been carefully edited again by a native English speaker.

We hope the revised version of the manuscript is now acceptable for publication in your journal.

I am looking forward to hearing from you soon.

With best wishes.

Yours sincerely,

Fei Pan

Associate chief physician

Corresponding author

We would like to express our sincere thanks to the reviewers for their constructive and positive comments.

Responses to Reviewer 1

To Reviewer 1

Specific Comments: I do not think the content of this paper offers novel concepts, low likelihood of being widely cited.

Answer: Thanks for your critical comments on our manuscript. We have taken the comments into account and partially revised the manuscript. We have added sections on endoscopic resection of ulcerative colitis-associated neoplasia, endoscopic and pathologic differential diagnosis of ulcerative colitis-associated and sporadic neoplasia, and anal cancer in patients with Crohn's disease. In addition, this manuscript provides an updated and comprehensive summary of the current state of research on colitis-associated colorectal cancer (CAC): (1) we have searched and summarized the extensive literature to present a more accurate description of the epidemiologic changes in CAC; (2) for the pathogenesis of CAC, we have proposed different mechanisms for colitis-associated colorectal cancer based on the latest research advances than previous literature; (3) we have invested a lot of time and management staff to understand and summarize the evidence of evidence-based medicine in CAC chemoprevention and guidelines and consensus statements around the world, including inflammatory bowel disease colonoscopic surveillance and surgical management. We hope you will find the revised manuscript acceptable.

Responses to Reviewer 2

To Reviewer 2

Specific Comments

1. I suggest that the authors describe concerning the endoscopic resection (ER) for UC-associated neoplasia.

Answer: Thanks for your comments. This part has been added in the revised version as "Previous viewpoints supported inflammatory bowel disease patients with non-adenoma-like dysplasia-related lesions or masses were recommended to undergo colectomy, whereas inflammatory bowel disease patients with adenoma-like dysplasia-related lesions or masses could be safely managed with polypectomy and continued surveillance in the absence of flat dysplasia elsewhere in the colon. The mainstream consensus is that endoscopic resection should be considered for all clearly delineated dysplastic-appearing lesions without evidence of invasive cancer or significant submucosal fibrosis. Endoscopic mucosal resection or endoscopic submucosal dissection may be considered for complex lesions not amenable to standard polypectomy, such as large and highly irregular lesions".

2. I suggest that the authors describe concerning the endoscopic and pathological differential diagnosis between UC-associated neoplasia and sporadic neoplasia.

Answer: Thanks for your comments. This part has been added in the revised version as "It is difficult to make a clear macroscopic distinction between colitis-associated colorectal cancer and sporadic colorectal cancer. In contrast to sporadic colorectal cancer, colitis-associated colorectal cancer appears to have distinguishing clinicopathologic features, evolving from a polymorphous dysplastic lesion rather than a polypoid adenoma. It is characterized by the lack of tumor histologic heterogeneity, tumor necrosis, Crohn's-like reaction, the presence of mucin, and signet ring cell differentiation and tumor well differentiation".

3. I suggest that the authors also give a brief description about anal cancer in patients with Crohn's disease, if possible.

Answer: Thanks for your comments. This part has been added in the revised version as "Specially, certain populations with autoimmune diseases are known to have a higher risk of developing anal cancer than average, such as ulcerative colitis patients with an incidence rate of 276167 person-years and

Crohn's disease patients with an incidence rate of 614830 py".

4. In the section of CAC SCREENING AND SURVEILLANCE, I suggest that "LDG" is a misspelling for "LGD".

Answer: Thanks for your careful review. Correction has been made in the revised version.

Responses to Reviewer 3

To Reviewer 3

Specific Comments: it is a well written manuscript.

Answer: We thank the reviewer for carefully reading our manuscript and providing the above positive comments.